

### REMARKS

Applicant requests reconsideration of the application in view of the following remarks.

The Examiner and Applicant interpret the gist of the present invention and the gist of the citations differently. Therefore, Applicant respectfully submits the following explanations to be considered by the Examiner.

**1. The invention in view of the prior art**

The present invention is directed to a process for the preparation of a polymer network having pores. In said pores a given substrate can be selectively bound, usually in a reversible way, i.e., such a network can be used in separation or recognition processes and the like (application, page 1, lines 4 to 12).

In this context, reference is made to a process of the prior art which is disclosed in WO93/09075 (cited in the application). Therein, a monomer is polymerized and simultaneously crosslinked in the presence of a substrate (here an optically pure enantiomer of the derivative to be separated). As the result, a molecular imprint of the optically pure enantiomer is formed in the polymer by non-covalent interaction between the polymer and said enantiomer. Subsequently, said substrate is removed by extraction with a suitable solvent. Then the molecular imprint can be used to separate said substrate from product mixtures (e.g. a racemic mixture containing said enantiomer) by chromatographic methods, i.e., the formed network having pores can be used in separation or recognition processes.

Instead of the term "substrate", the present invention uses the term "template" for the moiety that directs the (final) structure of the polymer containing the molecular imprint. As is known in this field of chemistry, a substrate or print molecule as termed in the WO93/09075 is often also termed as a "template" or a "template compound". An overview from the year 1997 which was readily found by Google internet search using the search terms "template and monomer" is attached hereto. Here, on page 2, Fig. 1, the principle of the imprinting process using a polymerizable monomer and a template is shown. The target molecule to be recognized is used to create its own recognition site. Accordingly, the target molecule is termed as a "template". Therefore, this term was already well known in the art before the priority date of the present application (November 30, 1998). The skilled person would always contemplate the term "template" in connection with assembling the molecular cast or molecular recognition as outlined in the overview. The skilled person would also learn from said document that the term "template"

comprises a variety of compounds. Also the present invention outlines that the template can comprise a variety of substances, i.e., it can both be a chemical compound and a biological structure, such as microorganisms, etc. (application, page 2, lines 29 to 34; step (ii) of claim 25; step (i) of claim 39).

In view of the drawbacks of the imprinting technique which are outlined on page 1, lines 21 to 29 of the present application, the invention provides an improved process not having said mentioned disadvantages.

This is achieved by processes disclosed in independent claims 25 and 39.

#### 1.1 Claim 25

Claim 25 reads:

A process comprising:

- (i) crosslinking a polymer; and
- (ii) adapting the conformation of the polymer obtained from (i) to a template dissolved or suspended in a solvent by interacting the polymer with the template, so as to increase the interaction enthalpy between the conformation and the template by more than 0.1 kcal/mole, the template being a chemical compound or a biological structure.

This process differs from the known processes of the above mentioned prior art in that instead of a monomer which is polymerized in the presence of the template in order to create recognition sites in a polymer, in step (i) a template interacts with an already crosslinked polymer (from step (i)), wherein the conformation of the crosslinked polymer is adapted to the template. This means that in the process of the present invention for the adaptation a structure is used which is already preorganized, i.e., the crosslinked polymer, instead of a monomer as used in the prior art as discussed above. The limitation regarding the interaction enthalpy excludes unspecific adaptations of the conformation of the crosslinked polymer which would be useless for a recognition process.

#### 1.2 Claim 39

Claim 39 reads:

A process comprising:

- (i) adapting the conformation of a polymer to a template by interacting the polymer with the template, the template being a chemical compound or a biological structure;
- (ii) crosslinking the polymer obtained from (i); and

(iii) exposing the polymer obtained from (ii) to the template for the polymer to preferentially attract and adhere the template to the polymer.

This process differs from the known processes of the above mentioned prior art in that instead of a monomer which is polymerized in the presence of the template, a template interacts with a polymer, wherein the conformation of the polymer is adapted to the template (step (i)). Subsequent to the adaptation, the adapted conformation of the polymer is fixed by crosslinking (step (ii)). Step (iii) discloses nothing else but that the created recognition site in the polymer according to step (ii) can be used to recognize the template that was used to create its own recognition site, e.g. in processes such as separation or recognition or the like. This inherently implies that the template is removed before carrying out step (iii). The skilled person would contemplate such a removal step in knowledge of the prior art.

## **2. Examiner's objections**

### **2.1 The cited prior art**

Examiner cites Anseth and Lee. According to the Examiner, in view of Lee, Anseth allegedly renders the present invention obvious (point 7).

Anseth teaches a process where sebacic acid (SA) or 16-bis-(p-carboxyphenoxy)-hexane (CPH), or oligomers thereof, are reacted with methacrylic anhydride, yielding the respective mixed anhydride functionalized monomers. The mixed anhydride functionalized monomer from the reaction between sebacic acid (SA) and methacrylic acid is termed MSA, the mixed anhydride functionalized monomer from the reaction between 16-bis-(p-carboxyphenoxy)-hexane (CPH) and methacrylic acid is termed MCPH. Subsequently, the mixed anhydride functionalized monomers can be crosslinked to form the respective polymer networks (reaction scheme at the bottom of columns 3 and 4 and column 4, line 29, through col. 5, line 25). The functionalized monomers can be applied in vivo to a site where an orthopedic implant is needed, and they can be crosslinked to form a biodegradable implant such as a rod, pin or plate (abstract). For the crosslinking reaction, Anseth uses UV light or a particular polymerization catalyst for the polymerization process (column 5, line 26 to 34).

The crosslinking step as taught by Anseth formally corresponds to step (i) of claim 25 and to step (ii) of claim 39 provided the crosslinking of the final polymer would be carried out in the presence of a template.

Applicant respectfully disputes the Examiner's assertion that Anseth discloses a template. With all due respect, Applicant believes that Examiner has misinterpreted the process as taught by Anseth or has interpreted said process in a manner the skilled person would not do.

It is known in the polymer field that that the crosslinking of polymers using crosslinkers, such as the crosslinking of styrene-based polymers with divinylbenzene, usually results in polymer networks, where the pores (recognition sites) are randomly shaped and randomly sized. Because MCPH acts as a crosslinker, the skilled person would assume that a process where the mixed anhydride functionalized monomers are crosslinked with MCPH also results in polymer networks, where the pores (recognition sites) are randomly shaped and randomly sized. After the crosslinking reaction, MCPH is an integral part of the polymer network which can not be removed unless the network is destroyed, also indicating that MCPH is not a template in the meaning as pointed out in the pertinent prior art.

In contrast to the crosslinking effect of MCPH in the process as taught by Anseth, the template as understood in the present application and in the related prior art mentioned above, guides the formation of the pores (recognition sites) in a manner so as to adapt the shapes and sizes to the shape and size of the template itself.

Even Anseth's object (tooth) the polymer is applied to and Anseth's drug that is incorporated into the prepolymer and in the resulting crosslinked polymer are not templates, as explained below.

## **2.2 The object the polymer is applied to**

For example, in a dental application, the tooth is covered with the mixed anhydride functionalized monomers which, subsequently, are crosslinked to produce the desired shape (application, column 6, line 56, to column 7, line 10).

For in vivo applications, the use of a solvent as taught by step (ii) of claim 25 of the present application, would not be possible due to possible harmful interaction with tissue. Further, the tooth would be insoluble in the solvent. Therefore, Anseth neither teaches nor suggests step (ii) of claim 25.

Additionally, claim 25 of the present invention requires the crosslinking of the polymer in step (i) prior to the adaptation in step (ii), whereas the crosslinking according to Anseth is performed after the adaptation. Therefore, Anseth neither teaches nor suggests the sequence of step (i) and step (ii) of the claimed process as disclosed in claim 25 of the present invention.

After placing the polymer on the tooth, the tooth is not removed, which would be done if the tooth really would act as a template. Otherwise the polymer containing the recognition site that is

created by the template could not be used to preferentially attract and adhere the template to the polymer as taught by step (iii) of claim 39 of the present invention. Therefore, Anseth neither teaches nor suggests the recognition process of step (iii) of claim 39.

### **2.3 The incorporated drug**

In the drug delivery application, the drug is incorporated before or after the crosslinking step into the prepolymer/polymer.

If a drug is added to the prepolymer prior to the crosslinking step, then Anseth teaches away from claim 25 of the present invention. That is because the process according to claim 25 requires the adaptation of a template subsequent to the crosslinking step as taught by the sequence of step (i) and (ii), but not prior to the crosslinking step (i).

If the drug is incorporated into the polymer after the crosslinking step -- although Anseth does not disclose any method how to perform such a step -- the drug has to be reversibly removed from the polymer in order to be able to function as template in the meaning as outlined in the pertinent prior art (point 1). However, the skilled person would assume that the polymer releases the drug only upon biodegradation of the polymer. Therefore, the drug would not be able to regain its former position in the polymer, and the polymer would not exhibit any selectivity for this drug. Further, Anseth's polymer is not intended to attract and adhere the drug during this application. To the contrary, the drug has to interact with bone, tissue or the like of the patient to be treated in a stronger manner than with the polymer, otherwise no therapeutic or diagnosis efficacy would be effected. Additionally, Anseth does not teach or suggest any process or method how to apply a drug to the stable crosslinked and dense polymer which is surrounded by tissue. Therefore, the drug does not fulfill the prerequisite to act as a template due to the non-reversible binding to the polymer. Thus, Anseth neither teaches nor suggests to use a template as taught in step (ii) of the process of claim 25 of the present application.

Since Anseth's polymer is not used to preferentially attract and adhere the drug to the polymer after the assumed drug was released by the polymer, Anseth also neither teaches nor suggests the recognition process of step (iii) of claim 39,

### 3. Conclusions

Knowing the teaching from the prior art as taught by the above template references, the skilled person would not assume MCPH to have the function of a template in the process as taught by Anseth. He would assume that MCPH is a mere crosslinker. Anseth provides no incentive to prepare a polymer network which can be used for recognition processes because Anseth teaches only a process for the preparation of biodegradable polymer networks for dental and orthopedic applications (implants). By contrast, the present application is specifically directed to processes for the manufacture of polymer networks for separation and recognition processes and the like as taught by independent claims 25 and 39. The technical fields according to the Anseth reference and according to the present invention are completely different from each other. The skilled person would consider the Anseth reference not to be relevant for the present invention.

Also, the tooth and drugs in Anseth's patent do not fulfill the requirements to act as a template in a polymer-template interaction as understood in the pertinent prior art and as taught by claims 25 and 39.

Due to the reasons outlined above, Applicant holds the opinion that the Anseth reference is irrelevant for the present invention. In view of this, the Lee reference can also be disregarded, because Lee only teaches that polymer networks can be prepared in a solvent.

### 4. Summary

Conclusively, independent claims 25 and 39 are novel and nonobvious as outlined in the above. Therefore, the other claims which are directly or indirectly dependent on claims 25 and 39 are also novel and nonobvious.

Therefore, the application is in condition for allowance, and allowance is requested.

Respectfully submitted,

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Date: 10/31/06